Equine Babesiosis, Equine Theileriosis, Biliary Fever

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**IOWA STATE UNIVERSITY®** 

College of Veterinary Medicine lowa State University Ames, Iowa 50011 Phone: 515.294.7189 Fax: 515.294.8259 cfsph@iastate.edu www.cfsph.iastate.edu



Iowa State University College of Veterinary Medicine www.cfsph.iastate.edu/IICAB/

#### **Importance**

Equine piroplasmosis is a tick-borne protozoal infection of horses. Piroplasmosis may be difficult to diagnose, as it can cause variable and nonspecific clinical signs. The symptoms of this disease range from acute fever, inappetence and malaise, to anemia and jaundice, sudden death, or chronic weight loss and poor exercise tolerance. Piroplasmosis is a major constraint to the international movement of equines. Although this disease was formerly endemic in Florida, the organisms were eradicated by the 1980s and piroplasmosis is considered to be an exotic disease in the United States. However, false negatives can occur in the complement fixation test, which was used for import testing until 2005, and there is a possibility that some horses in the U.S. might be inapparent carriers. In 2008, an outbreak occurred at a facility in Florida, highlighting the need to maintain constant vigilance for this disease.

#### **Etiology**

Equine piroplasmosis results from infection by the protozoa *Babesia caballi* or *Theileria equi* (formerly *Babesia equi*). Both organisms belong to the phylum Apicomplexa and order Piroplasmida. They can infect an animal concurrently.

Other related protozoa such as *Babesia bovis* (the organism that causes bovine babesiosis) have been reported rarely in horses.

#### **Species Affected**

Equine piroplasmosis affects horses, mules, donkeys and zebras. Zebras are an important reservoir for infection in Africa.

#### **Geographic Distribution**

The parasites that cause equine piroplasmosis are endemic in many tropical and subtropical regions including parts of Africa, the Middle East, Asia, Central and South America, the Caribbean and Europe. To a lesser extent, they may be found in temperate areas. *T. equi* is thought to have a wider distribution than *B. caballi*. Australia, New Zealand, Canada, Japan and some other countries are free of these parasites. Equine piroplasmosis was eradicated from the United States by the 1980s, and it is considered to be an exotic disease. However, false negatives can occur in the complement fixation test, which was used for import testing in the U.S. until 2004/2005, and there is a possibility that some horses might be inapparent carriers. Other piroplasmosis-free countries that used this test could also have some carriers.

#### **Transmission**

*B. caballi* and *T. equi* are transmitted by ticks, which become infected when they ingest parasites in the blood of infected equids. Approximately 14 species of ticks in the genera *Dermacentor*, *Hyalomma* and *Rhipicephalus* can be vectors for these organisms; however, the epidemiological significance of some species is unknown. Potential tick vectors for *T. equi* and *B. caballi* exist in the U.S.

Although ticks are biological vectors for both T. equi and B. caballi, differences in these parasites' replication cycles can affect their methods of transmission. Inside the tick, Babesia zygotes multiply as 'vermicules,' which invade many of the tick's organs including the ovaries, and Babesia species are readily passed to the next generation of ticks in the egg (transovarial transmission). When an infected larval, nymphal or adult tick of the next generation attaches to a new host, the parasite is stimulated to undergo its final maturation, allowing it to infect the host. In contrast, Theileria zygotes do not multiply in the tick, and transovarial transmission of T. equi is uncertain or absent. Ticks that transmit this organism can become infected as larvae and transmit the infection as nymphs, or they can become infected as nymphs and transmit the infection as adults (transstadial transmission). In some species of ticks such as Rhipicephalus microplus (formerly Boophilus microplus), T. equi can also be transmitted by the same tick stage that acquired the parasite (intrastadial transmission); whether this occurs in other species of ticks is unknown. Ticks infected with Theileria lose these parasites after transmission. Like B. caballi, T. equi parasites only stimulated to complete their maturation after the tick attaches to feed. For this reason, a tick infected with either organism must remain attached to the host for a time

before it becomes infective; often, *B. caballi* and *T. equi* are transmitted after the tick has been attached for a few days. Equine piroplasmosis can also be transmitted directly between animals by contaminated needles and syringes, or by blood transfusions.

After recovery, horses may become carriers for long periods. Animals infected with *B. caballi* can remain carriers for up to 4 years, but might be able to clear the organism eventually. Equids infected with *T. equi* appear to remain permanently infected. Parasitemia is often absent in carriers, but can reoccur after immuno-suppression or strenuous exercise. *T. equi* can be passed to the foal *in utero*, and some foals can be healthy carriers. Transplacental transmission of *B. caballi* has rarely been reported, and some sources consider the evidence for this route to be unreliable.

#### **Incubation Period**

The incubation period for equine piroplasmosis is 12 to 19 days when it is caused by *T. equi*, and 10 to 30 days when it is caused by *B. caballi*.

#### **Clinical Signs**

The clinical signs of piroplasmosis are variable and often nonspecific. *T. equi* tends to cause more severe disease than *B. caballi*.

In rare peracute cases, animals may be found dead or dying. More often, piroplasmosis presents as an acute infection, with fever, inappetence, malaise, labored or rapid respiration and congestion of the mucus membranes. The feces may be small and dry, but diarrhea has also been reported. Anemia, thrombocytopenia, hemoglobinuria, sweating, petechial hemorrhages on the conjunctiva, a swollen abdomen, and posterior weakness or swaying may also be seen. Subacute cases have similar but less severe clinical signs. The fever may be intermittent, and animals may show weight loss, signs of mild colic, and mild edema of the distal limbs. The mucus membranes in subacute cases can be pink, pale pink or yellow, and they may have petechiae or ecchymoses. In chronic cases, common symptoms include mild inappetence, poor exercise tolerance, weight loss, transient fevers and an enlarged spleen (palpable on rectal examination). Some infected mares, including carrier mares, may abort or pass T. equi to their offspring. Foals infected in utero may be weak at birth, and rapidly develop anemia and severe jaundice. In other cases, these foals can be healthy carriers.

Asymptomatic carriers can develop clinical signs after immunosuppression or strenuous exercise.

#### Post Mortem Lesions di Click to view images

In acute cases, the animal is usually emaciated, jaundiced and anemic. The liver is typically enlarged and may be either dark orange-brown or pale from anemia. The spleen is enlarged. The kidneys may be pale and flabby, or they may be dark red or black if the animal had

hemoglobinuria. Petechial hemorrhages may be seen in the kidneys and subepicardial and subendocardial hemorrhages in the heart. Secondary infections may cause edema, emphysema or signs of pneumonia in the lungs.

#### **Morbidity and Mortality**

In some areas, equine piroplasmosis is most common in the summer and fall; however, even in these regions, cases can occur throughout the year. In some endemic areas where tick control is not practiced, nearly all horses are eventually exposed to *B. caballi*. Reported case fatality rates for equine piroplasmosis vary; one source suggests that the mortality rate can vary from less than 10% to as high as 50%.

#### **Diagnosis**

#### Clinical

Equine piroplasmosis should be suspected in horses with anemia, jaundice and fever; however, the clinical signs are often variable and nonspecific.

#### Differential diagnosis

The differential diagnosis for piroplasmosis includes surra, equine infectious anemia, dourine, African horse sickness, purpura hemorrhagica, and various plant and chemical toxicities.

#### Laboratory tests

Equine piroplasmosis can be diagnosed by identification of the organisms in Giemsa stained blood or organ smears. *B. caballi* merozoites are joined at their posterior ends, while *T. equi* merozoites are often connected in a tetrad or "Maltese cross." *T. equi* can often be found in the blood in acute infections, but may be very difficult to find in carrier animals. *B. caballi* can sometimes be difficult to find even in acute disease. In carriers or other animals with low parasitemia, thick blood films can sometimes be helpful.

Because organisms can be difficult to detect in carriers, serology is often used for diagnosis. Serological tests include complement fixation (CF), indirect fluorescent antibody (IFA) and various enzyme-linked immunosorbent (ELISA) assays. Immunoblotting (Western blotting) can also be used, and an immunochromatographic test for *T. equi* has been described. The complement fixation test can be affected by natural anticomplementary activity in serum, as well as drug treatment or other factors; some carriers can be negative in this test. Animals do not become CF-positive for at least a month after inoculation. For these reasons, the IFA test and competitive ELISA (C-ELISA) have replaced complement fixation for import testing The IFA test can distinguish *T. equi* from *B. caballi*.

Polymerase chain reaction (PCR) assays are available in some laboratories. Additional molecular techniques include nested PCR, multiplex PCR and loop-mediated isothermal amplification (LAMP).

Other methods of diagnosis are *in vitro* culture and the inoculation of a susceptible (preferably splenectomized) animal with blood from a suspected carrier. In addition, pathogen-free vector ticks can be fed on a suspect animal, and *B. caballi* or *T. equi* identified either in the tick or after the tick has transmitted the infection to a susceptible animal. These methods can detect *B caballi* and *T. equi* when other techniques do not find the parasites. They can be particularly useful in carriers.

#### Samples to collect

Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease. Animal *Babesia* or *Theileria* species have been implicated in human infections; samples should be collected and handled with all appropriate precautions.

Several thick and thin blood smears or an unclotted blood sample should be taken from live animals. Blood smears are optimally made from superficial skin capillaries during the acute phase of the disease. If possible, these samples should be collected during a rise in body temperature. Organ smears can be collected at necropsy. Slides should be air-dried and fixed in methanol. Serum should also be taken for serology. Larger amounts of blood are necessary for transmission tests to a susceptible horse; one source recommends that 500 ml uncoagulated blood (with antibiotics added) should be collected. Samples should be transported on wet ice or with frozen gel packs.

# Recommended actions if equine piroplasmosis is suspected

#### Notification of authorities

Equine piroplasmosis is exotic to the U.S. and must be reported immediately to state or federal authorities.

Federal: Area Veterinarians in Charge (AVIC):

http://www.aphis.usda.gov/animal\_health/area\_offices/

State Veterinarians:

http://www.usaha.org/Portals/6/StateAnimalHealthOfficials.pdf

#### Control

Carrier animals or infected ticks can introduce equine piroplasmosis into new regions. Equids are usually tested for this disease during importation. IFA and ELISA tests are highly sensitive, but complement fixation may not detect all carriers.

Disinfectants and sanitation are not generally effective against the spread of tick-borne infections. However, eliminating contact with ticks and preventing the transfer of blood from one animal to another are vital. In endemic areas, the use of acaricides, together with frequent examination of the animal and immediate removal of any

ticks (parasite transmission does not occur immediately), may help prevent infection.

If an infected animal is discovered in a piroplasmosisfree region, the animal must be quarantined and kept from all contact with ticks. Strict precautions should be taken to prevent contact between horses and ticks, whenever carriers are admitted to a piroplasmosis-free country for an international competition. These measures can include spraying the premises repeatedly with acaricides, eliminating vegetation from these areas, and maintaining infected horses in a separate quarantine area except during competition and other specified activities. Pets, wildlife and rodents should be excluded from these areas. Horses should be inspected daily for ticks and may be treated with acaricidal sprays and shampoos. Ticks could hide in animal wastes, which should be destroyed and not allowed to leave the quarantine area. Sentinel horses may be used to monitor the effectiveness of these controls.

Treatment can suppress clinical signs, but the currently available treatments are ineffective in clearing *T. equi* from carriers. Some studies have suggested that treatment could eliminate *B. caballi* from infected horses; however, in a recent study, this organism persisted in carriers after even high dose treatment with imidocarb. Although this drug could temporarily clear the parasites and resulted in transiently negative PCR results, *B. caballi* DNA was found in horses after the treatment ended. There is no vaccine for either *B. caballi* or *T. equi*.

#### **Public Health**

Some species of *Babesia* or *Theileria* can occasionally infect species other than their usual host, including humans. To date, the most important pathogens for humans appear to be the bovine pathogen *B. divergens* in Europe and the rodent species *B. microti* in the U.S. Although *B. caballi* or *T. equi* may have been implicated in a few human infections in the past, these organisms do not seem to be important zoonoses. However, human babesiosis is still incompletely understood, and the possibility of infection with these organisms has not been ruled out.

Humans usually acquire Babesia species from ticks, but infections have also been reported after receiving transfusions of infected blood. The form of the disease can with the species of Babesia immunocompetence of the host. In most healthy, immunocompetent individuals, babesiosis tends to be mild or asymptomatic, and the symptoms often resolve without treatment. B. divergens has been mainly associated with illness in splenectomized individuals, and B. microti infections are often diagnosed in older patients. In humans, babesiosis is characterized by fever, chills, anemia, fatigue and headache. Jaundice, hemoglobinuria, neurological signs, and complications such as congestive heart failure, disseminated intravascular coagulation, kidney failure or respiratory distress syndrome may also be seen. Some infections can be rapidly progressive and fatal. Coinfection

with *Babesia* can also increase the severity of diseases such as Lyme disease. Human babesiosis can be treated with antibiotics.

#### **Internet Resources**

- The Merck Veterinary Manual <a href="http://www.merckvetmanual.com/mvm/index.jsp">http://www.merckvetmanual.com/mvm/index.jsp</a>
- United States Animal Health Association.

  Foreign Animal Diseases

  <a href="http://www.aphis.usda.gov/emergency-response/downloads/nahems/fad.pdf">http://www.aphis.usda.gov/emergency-response/downloads/nahems/fad.pdf</a>
- World Organization for Animal Health (OIE) http://www.oie.int
- OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
  <a href="http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/">http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/</a>
- OIE Terrestrial Animal Health Code <a href="http://www.oie.int/international-standard-setting/terrestrial-code/access-online/">http://www.oie.int/international-standard-setting/terrestrial-code/access-online/</a>

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